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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/846,893	JUDICE ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 14-17* is/are pending in the application.

4a) Of the above claim(s) *14-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☒ Claim(s) *1-10 and 14-17* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 & 6-7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' preliminary amendment filed 15 May 2003 (Paper No. 10) which cancels claims 11-13 and 18-19 and amends claims 1, 5-6 and 15-17 has been entered. The following Office action is applicable to the pending claims 1-10 and 14-17.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10, drawn to a pharmaceutical composition comprising a cyclodextrin and a lapidated glyco-peptide antibiotic, are classified in class 514, subclasses 8, 58 and 183, and class 530, subclass 395.

II. Claims 14-17, drawn to a method of treating a disease state in a mammal comprising administering to the mammal the pharmaceutical composition thereof and a method of reducing tissue accumulation in a mammal of a lapidated glyco-peptide antibiotic (i.e., reducing cytotoxicity of the antibiotic), are classified in class 514, subclasses 8 and 58.

The inventions are distinct, each from the other because of the following reasons:

Invention I is related to Invention II as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the component of the pharmaceutical composition, i.e., cyclodextrin can be used to assess a real time interaction between cyclodextrin and cyclodextrin glycosyltransferase on a gold surface in a surface plasma resonance instrument.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art shown by their different classification, art recognized divergent subject matter, separate search, restriction for examination purposes as indicated is proper.

During a telephone conversation with Jeffrey Hagenah on August 25, 2003 a provisional election was made with traverse to prosecute the Group I, claims 1-10. Affirmation of this election must be made by applicants in replying to this Office action. Claims 14-17 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification/Claim/Objections

The disclosure is objected to because of the following informalities:

In page 16, line 23, "-(CH(NH_2)CH2-)" should be changed to "-(CH(NH_2)CH_2-)".

In page 36, line 4, "HPLC" should be spelled out in full at the first instance of use.

In claim 6, item (c), a verb is missing after "provided that ..."

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 recites "or a pharmaceutical acceptable salt thereof"; the recitation is unclear as to what component: (i) "the cyclodextrin" or (ii) "the antibiotic", or the component in combination of (i) and (ii), the said salt refers. See also claim 5 and claim 6, item (a). The dependent claims are also rejected.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 5 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Patel, M. G. et al. (US Pat. No. 5776912).

Patel et al. teach an aqueous pharmaceutical composition (see abstract) comprising lipophilic oligosaccharide (glycopeptide) antibiotic and cyclodextrin (see column 1, lines 37-43), which anticipates claims 1 and 5 of the instant application. Since the Patel et al. teaching is directed to aqueous composition, i.e., water is solvent for the composition, the above teaching is also applicable to the instant claim 2.

Additionally, Patel et al. teach that cyclodextrin is hydroxypropyl-β-cyclodextrin (see column 1, lines 42-43), which meets the limitation set forth in claims 7-8.

Thus, Patel et al. patent anticipates claims 1-2, 5 and 7-8 of the instant application.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Patel, M. G. et al. (US Pat. No.5624914).

Patel et al. teach an aqueous pharmaceutical composition comprising lipophilic oligosaccharide (glycopeptide) antibiotic and cyclodextrin (see the patent claims 7, 11 and 13), which is applied to claim 1 of the instant application.

Patel et al. teach the pharmaceutical composition comprises water (see example 3A, column 8, lines 37-39, and column 22,lines 8-9), as applied to the instant claim 2. Since the water is an aqueous cyclodextrin carrier, the above the Patel et al. teaching is applied to the instant claim 5.

Patel et al. teach the compositions of the invention in the form of a lyophilized powder (see column 22, lines 19-22), as applied to the instant claims 3-4.

Patel et al. teach an aqueous pharmaceutical composition comprises the lipophilic oligosaccharide (glycopeptide) antibiotic and a pharmaceutical acceptable carrier (see the patent claims 7 and 11). Also, Patel et al. teach that the use of sterilized water as a carrier is preferred (see column 21, line 66) and that the composition comprises the cyclodextrin preferably 1-5% (see column 22, lines 32-33), i.e., the water content of the composition is thereof about 95-99%. The Patel et al. teaching meets the limitations set forth in the instant claim 6.

Patel et al. teach that cyclodextrin is hydroxypropyl-β-cyclodextrin (see the patent claim 17), which meets the limitation set forth in the instant claims 7-8.

Also, Patel et al. teach the composition comprises the cyclodextrin of less than 20 % by weight (see column 22, line 39), which is applied to the limitation of the instant claims 9-10.

Therefore, the Patel et al. patent anticipates claims 1-10 of the current application.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 5 and 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberto, D. P. et al. (EP 0463653) as is evidenced by Hunt, A. H. et al. (US Pat. No. 4639433).

Claims 3-4, 6 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberto, D. P. et al. (EP 0463653) as is evidenced by Hunt, A. H. et al. (US Pat. No. 4639433) as applied to claims 1-2, 5 and 7-8 above, and further in view of Hirai S.-I. et al. (EP 0094157)

and Rubinfeld J. (US Pat. No. 6048845) and Pea F. et al. (*J. Antimicrob. Chemother.* (2000) 45, 329-335).

Roberto et al. a pharmaceutical composition comprising cyclodextrin, a drug molecule and a pharmaceutical carrier (see the patent claims 1-3), wherein the cyclodextrin is hydroxypropyl-β-cyclodextrin (i.e., 2- hydroxypropyl cyclodextrin) (see the patent claim 6) and the drug molecule is a cyclic peptide antibiotic (see column 5, line 16), as applied to the instant claims 1-2, 5 and 7-8. Note that the cyclic peptide antibiotic encompasses glyco-peptide antibiotic which includes lipid modified glyco-peptide antibiotics, i.e., the lapidated glyco-peptide antibiotic is a type of cyclic peptide antibiotic as is evidenced by the following Hunt et al. teaching.

Hunt et al. teach a pharmaceutical composition comprising a glyco-peptide antibiotic derivative (see abstract and the patent claims 1, 8-9 and 26) of the alkanoic acid modification in which the position R_2 and R_3 form an acyl (i.e., R-CO-) side chain (see column 5, lines 11-15), which is a lipidated derivative of the antibiotic. Thus, the Robert et al. patent together with the Hunt et al. patent are obvious variation over claims 1, 5 and 6 of the current application.

Roberto et al. and Hunt et al. do no explicitly teach the physical for of the composition and weight percentage of the components that constitute the composition thereof.

Hirai et al. teach a pharmaceutical composition comprising cyclodextrin and an antibiotic (see the patent claims 1-3) and teach that the cyclodextrin content in the composition is preferably about 2-10% by weight (see page 18, lines 11-14), as applied to the instant claims 9-10.

Also, Hirai et al teach a freeze-dried (i.e., lyophilized) powdery composition (see page 7, line 11), as applied to the instant claims 3-4.

Further, Hirai et al. teach the lipid pharmaceutical composition prepared in water comprising a drug (e.g., antibiotic) and cyclodextrin (see page 8, lines 8-12) wherein the antibiotic is 0.05-40 w/v percent (see page 7, line 25) typically having effective dose 0.05-1 g (see page 18, line 9), and cyclodextrin 2-20 w/w percent (see page 18,lines 11-13). Therefore, water content of the composition would be 40 to 98 weight percent, which meets the limitation set forth in claim 6 of the current application.

It would have been obvious to one of ordinary skill in the art at the time the invention was made would have combined the teachings of the above references because Robert et al. teach a pharmaceutical composition comprising cyclodextrin and peptide antibiotic, Hunt et al. teach the type of the peptide antibiotic is a lipidated glyco-peptide antibiotic, and Hirai et al. teach a pharmaceutical composition comprising cyclodextrin and the bioactive component, e.g., peptide antibiotic, the weight percent of the cyclodextrin and freeze-dried power form of the composition. When combined, there would be the following advantages: (i) high level of bioavailability (see page 15, line 25), (ii) improve drug efficacy in view of biological half-life of the administrated drug (see page 18, lines 30-34), (iii) low cytotoxicity (see page 18,lines 34-38) and (iv) permutable repeated dose regimens (see page 18, lines 21-38), as taught by Hirai et al. Cyclodextrin-formulated pharmaceutical composition has an especial benefit for formulating cytotoxic drug, e.g., antibiotic such as glycopeptide antibiotic, i.e., bleomycins (see abstract and column 11, lines 48-53 of the Rubinfeld et al. patent), and, it has been known in the prior art of record that use of cyclodextrin in the pharmaceutical composition reduces the cytotoxicity of the

composition (see the Roberto et al. teaching, especially abstract), which would be, therefore, noticeably advantageous to the glyco-peptide antibiotics which have undesirable nephrotoxicity, e.g., vancomycin (see the Pea et al. reference, at page 330, the left column, lines 3-4).

Given the above motivation, one of ordinary skill in the art would have combined the teachings of the above references to develop the pharmaceutical composition comprising the potential toxic glyco-peptide antibiotic and the cyclodextrin for achieving high pharmaceutical efficacy and lower cytotoxicity of the antibiotics. Therefore, the claimed invention was *prima facie* obvious to make and use the invention at the time it was made.

Provisional Rejection - Obviousness Type Double Patenting

Claims 1-2, 5 and 17-18 of this application conflict with Claims 10, and 17-18 of Application No. 09776466. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 5 and 17 are provisionally rejected under the judicially created doctrine of double patenting over claims 10 and 17 of copending Application No. 09674266. This is a provisional double patenting rejection because the conflicting claims have not in fact been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows:

Claims 10 and 17 of Application 09776466 discloses a pharmaceutical composition comprising a lapidated glycopeptide antibiotic, and a pharmaceutical acceptable carrier thereof which is the common subject matter of the instant claim 1. Since Application 09776466 is directed to an aqueous composition wherein the pharmaceutical carrier is water (see [0310]), the 09776466's disclosure is an obvious variation over the instant claims 2 and 5.

Claims 17 of Application 09776466 are the obvious variation over the instant claims 7 and 8 because 09776466 sets froth that, in a preferred embodiment, the cyclodextrin is hydroxypropyl-β-cyclodextrin (see [0191]).

Thus, the instant application and Application 09776466 claims are obvious variation, and they are not patentably distinct from each other.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703 308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Samuel Wei Liu, Ph.D.

August 27, 2003

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